REMARKS/ARGUMENTS

Claims 1-21 are pending in this application.

Declaration under 37 C.F.R. §1.132

Applicants submit herewith a declaration by Dr. Philip J. Barr, who is currently employed by Arriva Pharmaceuticals, Inc. (the Applicants).

I. Rejection under 35 U.S.C. §112, first paragraph - Definiteness

Applicants thank the Examiner for withdrawing the rejection of claims 13 and 14.

II. Double patenting rejection

Claims 1-21 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 6, 8, 9, 12, 29, and 32 of U.S. Application 10/579,088. The Examiner states that "[a]lthough the conflicting claims are not identical, they are not patentably distinct from each other . . . [and c]laims 1-21 herein and Claims 1-3, 6, 8, 9, 12, 29, and 32 are both directed to dry powder compositions comprising recombinant human alpha 1-antitrypsin. Applicants respectfully request that the Examiner hold this rejection in abeyance until a finding of allowable subject matter.

III. Rejection under 35 U.S.C. §112, first paragraph - Enablement

Claims 1-21 remain rejected under 35 U.S.C. §112, first paragraph allegedly for lack of enablement. Applicants traverse the rejection and maintain for the reasons on record and those described herein that when the proper legal standard is applied, the instant specification provides sufficient disclosure to enable a person of ordinary skill in the art to make and use the invention as presently claimed.

The Examiner argues that the disclosures of the specification and references cited by the Applicants are "not sufficient to enable the skilled artisan to make and use any human polypeptide having any α1-antitrypsin activity." (pages 5-6 of the Final Office Action). Applicants respectfully disagree and submit that based upon the specification and public knowledge at the time of filing, sufficient support is provided for the specific "non-glycosylated

recombinant human alpha 1-antitrypsin (rAAT)" that is recited in pending claim 1. As previously argued by Applicants, the present specification provides that rAAT "is a 395 amino acid protein of 44 kD, that is non-glycosylated and has an amino acid sequence identical to the human plasma protein (AAT) with the exception of an N-acetylmethionine residue at the amino terminus" (lines 6-10, page 1). As stated in paragraph 7 of the Declaration by Dr. Barr, a

> search on the Protein sequence database at http://www.ncbi.nlm.nih.gov/sites/entrez?db=Protein&itool=toolbar using the search criteria "plasma AND human[Organism] AND alpha-1-antitrypsin[Protein Name]" yielded two identical hits (Accession Nos. P01009 and AAB59375), each of which provides a 418 amino acid sequence designating the signal peptide as residues 1-24 resulting in a mature 394 amino acid polypeptide. The 394 amino acid sequence was also published in Figure 1 of Rosenberg *et al. Nature*, 312 (5989), 77-80 (1984). A person of ordinary skill in the art would appreciate that the rAAT referred to by the Applicants in the claims and specification corresponds to the human plasma protein (AAT) sequence provided in Accession Nos. P01009 and AAB59375, with the exception of an N-acetylmethionine residue at the amino terminus.

Applicants submit that a person of ordinary skill in the art would appreciate that the 395 amino acid sequence shown below in Figure 1 corresponds to the rAAT recited in the pending claims and described in the instant specification. Figure 1 shows the first 24 amino acids underlined (cleavable signal sequence), a bolded methionine (M) that is not in the natural sequence, and the 394 amino acids located C-terminal to the M residue.

Figure 1

MPSSVSWGILLLAGLCCLVPVSLA**M**EDPQGDAAQKTDTSHHDQDHPTFNKITPN
LAEFAFSLYRQLAHQSNSTNIFFSPVSIATAFAMLSLGTKADTHDEILEGLNFNLT
EIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSEGLKLVDKFLEDVKKLYHSE
AFTVNFGDTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFALVNYIFFKGKWE
RPFEVKDTEEEDFHVDQVTTVKVPMMKRLGMFNIQHCKKLSSWVLLMKYLGN
ATAIFFLPDEGKLQHLENELTHDIITKFLENEDRRSASLHLPKLSITGTYDLKSVLG
QLGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGTEAAGAMFLEAIPMS
IPPEVKFNKPFVFLMIEQNTKSPLFMGKVVNPTQK

The legal standard for determining enablement has been set forth previously (see page 12 of the October 10, 2008 Response). Applicants respectfully submit that upon application of the legal

standard, the pending claims meet the requirement for enablement. As explained above, the specification provides several identifying characteristics for rAAT, i.e., "a 395 amino acid protein of 44 kD, that is non-glycosylated and has an amino acid sequence identical to the human plasma protein (AAT) with the exception of an N-acetylmethionine residue at the amino terminus" [emphasis added] (lines 6-10, page 1). As explained in the Declaration by Dr. Barr, a person of ordinary skill in the art could readily use this information to identify the publicly available amino acid sequence corresponding to rAAT. Therefore, Applicants submit that the rejection of claim 1, and all claims depending therefrom, under 35 U.S.C. § 112, first paragraph are overcome, and the Examiner is respectfully requested to reconsider and withdraw these rejections.

IV. Rejection under 35 U.S.C. §112, first paragraph – Written description

Claims 1-21 remain rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants traverse the rejection and maintain for the reasons on record and those described herein that when the proper legal standard is applied, it is clear that the instant specification reasonably conveys to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

As previously described by Applicants, the factual determination in a written description analysis depends on the nature of the invention and the amount of knowledge imparted to those skilled in the art by the disclosure. *Union Oil v. Atlantic Richfield Co.*, 208 F.2d 989, 996 (Fed. Cir. 2000; *See also* M.P.E.P. §2163 II(A)). As discussed above, paragraph 6 of the Declaration by Dr. Barr provides that a

> person of ordinary skill in the art would appreciate that the rAAT referred to by the Applicants in the claims and specification corresponds to the human plasma protein (AAT) sequence provided in Accession Nos. P01009 and AAB59375, with the exception of an N-acetylmethionine residue at the amino terminus.

Upon taking into account the nature of the invention and level of knowledge in the relevant art, it is clear that Applicants are not required to recite the specific amino acid sequence for rAAT because this information could readily be obtained in the public domain by a person of ordinary skill in the art at the time of filing of the instant application. As such, Applicants request reconsideration by the Examiner and a withdrawal of the rejection.

V. Rejection under 35 U.S.C. §102(b) - Anticipation

Claims 1-19 and 21 remain rejected under 35 U.S.C. §102(b), allegedly for being anticipated by Eljamal et al. (U.S. Pat. No. 5,780,014). The Examiner states that "Eljamal et al teach that recombinant forms of α1-antitrypsin can be used in their method" (page 8 of the Final Office Action). Applicants respectfully disagree and continue to traverse the rejection. As currently amended, claim 1 recites a "non-glycosylated recombinant human alpha 1-antitrypsin" [emphasis added]. Eljamal et al. is silent regarding whether the recombinant AAT is glycosylated and therefore does not teach or suggest each and every element of the currently pending claims. As the reference does not teach or suggest each and every element of the currently pending claims, it cannot be used to assert an anticipation rejection. Applicants respectfully request reconsideration by the Examiner and a withdrawal of the rejection.

VI. Rejection under 35 U.S.C. §103(a)

Claim 20 remains rejected as being allegedly unpatentable over Eljamal et al. (U.S. Pat. No. 5,780,014) (hereinafter "Eljamal") in view of Millqvist-Fureby et al. (1999) Int'l. J. Pharmaceutics, 188:243-253 (hereinafter "Millqvist-Fureby"). The Examiner asserts it "is Eljamal that teaches use of a recombinant/ non-glycosylated α1-antitrypsin polypeptide" [emphasis added] (page 9 of the Final Office Action). Applicants respectfully disagree and continue to traverse the rejection for the reasons of record and the reasons provided herein. Claim 20 depends from independent claim 1 and therefore includes all the elements of claim 1. As discussed above, Eljamal is silent regarding whether the recombinant AAT is glycosylated and therefore does not teach or suggest each and every element of pending claim 20. As previously discussed by the

Applicants, Millqvist-Fureby et al. fails to cure the defects of Eljamal et al. because it is limited to the analysis of crystalline porcine trypsin 4500 K, which is manufactured by the extraction of its inactive precursor, trypsinogen, from porcine pancreatic tissue (see Novozymes product information sheet). As such, the trypsin disclosed in Millqvist-Fureby et al. is not recombinant, nor is there any indication it is non-glycosylated. As such, there is no teaching in either reference of a recombinant non-glycosylated AAT polypeptide. As the references do not teach or suggest each and every element of pending claim 20, a prima facie case of obviousness has not been established. Applicants respectfully request reconsideration and a withdrawal of the rejection.

Statement of Related Applications

Applicants ask the Examiner to consider the following cases which are related to the above application:

U.S. Patent No. 7,419,801 issued on September 2, 2008 entitled "Methods of Protein Production in Yeast";

U.S. Application Serial No. 12/217,612 filed July 7, 2008 entitled "Methods of Protein Production in Yeast";

U.S. Application Serial No. 11/077,276 filed March 5, 2005 entitled "Treatment of Chronic Obstructive Pulmonary Disease by Low Dose Inhalation of Protease Inhibitor";

U.S. Application Serial No. 10/579,088 filed November 11, 2004 entitled "Alpha 1-Antitrypsin Compositions and Treatment methods using such compositions";

U.S. Patent No. 7,247,704 issued July 24, 2007 entitled "Multifunctional Protease Inhibitors and their use in treatment of disease"; and

U.S. Application Serial No. 11/781,152 filed July 20, 2007 entitled "Multifunctional Protease Inhibitors and their use in treatment of disease".

CONCLUSION

The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. **50-4634** (referencing Attorney's Docket No. **ARR-0037-1.US (123887-182053)**). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Goodwin|Procter LLP

Date: September 4, 2009

By: _____
Jeffery P. Bernhardt (Reg. No. 54,997)

Goodwin Procter LLP
Customer No. 77845
135 Commonwealth Drive
Menlo Park, CA 94025-1105
650-752-3100
650-853-1038 (fax)

LIBC/3549023.1